

(b) In connection with its study of this problem, the Food and Drug Administration has obtained the views of medical authorities. It is the unanimous recommendation of the American Academy of Pediatrics, the American Association of Poison Control Centers, the American Medical Association, and the Medical Advisory Board of the Food and Drug Administration that ipecac syrup in 1 fluid ounce containers be permitted to be sold without prescription so that it will be readily available in the household for emergency treatment of poisonings, under medical supervision, and that the drug be appropriately packaged and labeled for this purpose.

(c) In view of the above recommendations, the Commissioner of Food and Drugs has determined that it is in the interest of the public health for ipecac syrup to be available for sale without prescription, provided that it is packaged in a quantity of 1 fluid ounce (30 milliliters), and its label bears, in addition to other required label information, the following, in a prominent and conspicuous manner:

(1) A statement conspicuously boxed and in red letters, to the effect: "For emergency use to cause vomiting in poisoning. Before using, call physician, the Poison Control Center, or hospital emergency room immediately for advice."

(2) A warning to the effect: "Warning—Keep out of reach of children. Do not use in unconscious persons. Ordinarily, this drug should not be used if strychnine, corrosives such as alkalis (lye) and strong acids, or petroleum distillates such as kerosene, gasoline, coal oil, fuel oil, paint thinner, or cleaning fluid have been ingested."

(3) Usual dosage: 1 tablespoon (15 milliliters) in persons over 1 year of age.

§201.309 Acetophenetidin (phenacetin)-containing preparations; necessary warning statement.

(a) In 1961, the Food and Drug Administration, pursuant to its statutory responsibility for the safety and effectiveness of drugs shipped in interstate commerce, began an active investigation of reports of possible toxic effects and renal damage due to misuse of the drug acetophenetidin. This study led to

the decision that there was probable cause to conclude that misuse and prolonged use of the drug were in fact responsible for kidney lesions and disease. The Commissioner of Food and Drugs, in December 1963, appointed an ad hoc Advisory Committee of Inquiry on Possible Nephrotoxicity Associated With the Abuse of Acetophenetidin (Phenacetin)-Containing Preparations. This committee, composed of scientists in the fields of pharmacology and medicine, on April 23, 1964, submitted its findings and conclusions in the matter and recommended that all acetophenetidin (phenacetin)-containing preparations bear a warning as provided in section 502(f)(2) of the Federal Food, Drug, and Cosmetic Act.

(b) On the basis of the studies made by the Food and Drug Administration and the report of the Advisory Committee, the Commissioner of Food and Drugs has concluded that it is necessary for the protection of users that the label and labeling of all acetophenetidin (phenacetin)-containing preparations bear a warning statement to the following effect: "Warning—This medication may damage the kidneys when used in large amounts or for a long period of time. Do not take more than the recommended dosage, nor take regularly for longer than 10 days without consulting your physician."

§201.310 Phenindione; labeling of drug preparations intended for use by man.

(a) Reports in the medical literature and data accumulated by the Food and Drug Administration indicate that phenindione, a synthetic anticoagulant drug, has caused a number of cases of agranulocytosis (with two fatalities). There are also reports implicating the drug in cases of hepatitis and hypersensitivity reactions. In view of the potentially serious effects found to be associated with preparations of this drug intended for use by man, the Commissioner of Food and Drugs will regard such preparations as misbranded within the meaning of section 502(f) (1) and (2) of the Federal Food, Drug, and Cosmetic Act, unless the label and labeling on or within the package from which the drug is to be dispensed, and

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any other labeling furnishing or purporting to furnish information for use of the drug, bear a conspicuous warning statement to the following effect: "Warning: Agranulocytosis and hepatitis have been associated with the use of phenindione. Patients should be instructed to report promptly prodromal symptoms such as marked fatigue, chill, fever, and sore throat. Periodic blood studies and liver function tests should be performed. Use of the drug should be discontinued if leukopenia occurs or if evidence of hypersensitivity, such as dermatitis or fever, appears."

(b) Regulatory action may be initiated with respect to preparations of phenindione intended for use by man found within the jurisdiction of the act on or after November 25, 1961, unless such preparations are labeled in accordance with paragraph (a) of this section.

§ 201.311 [Reserved]

§ 201.312 Magnesium sulfate heptahydrate; label declaration on drug products.

Magnesium sulfate heptahydrate should be listed on the label of a drug product as epsom salt, which is its common or usual name.

§ 201.313 Estradiol labeling.

The article presently recognized in The National Formulary under the heading "Estradiol" and which is said to be "17-cis-beta estradiol" is the same substance formerly recognized in the United States Pharmacopeia under the designation "Alpha Estradiol." The substance should no longer be referred to in drug labeling as "Alpha Estradiol." The Food and Drug Administration would not object to label references to the article as simply "Estradiol"; nor would it object if the label of a preparation containing this substance referred to the presence of "Estradiol (formerly known as Alpha Estradiol)."

§ 201.314 Labeling of drug preparations containing salicylates.

(a) The label of any oral drug preparation intended for sale without prescription and which contains any salicylate ingredient (including aspirin, salicylamide, other salicylates, and combinations) must conspicuously bear, on a clearly contrasting background, the warning statement: "Keep out of reach of children [highlighted in bold type]. In case of overdose, get medical help or contact a Poison Control Center right away," or "Keep out of reach of children [highlighted in bold type]," except that if the article is an aspirin preparation, it shall bear the first of these warning statements. Such a warning statement is required for compliance with section 502(f)(2) of the Federal Food, Drug, and Cosmetic Act and is intended to guard against accidental poisonings. Safety closures that prevent access to the drug by young children are also recommended to guard against accidental poisonings.

(b) Effervescent preparations and preparations containing paraminosalicylate as the only salicylate ingredient are exempted from this labeling requirement.

(c) Aspirin tablets sold as such and containing no other active ingredients, except tablets which cannot be readily subdivided into a child's dose because of their coating or size, should always bear dosage directions for each age group down to 3 years of age, with a statement such as "For children under 3 years of age, consult your physician." It is recommended that:

(1) Aspirin tablets especially made for pediatric use be produced only in 1¼-grain size to reduce the hazard of errors in dosage;

(2) By June 1, 1967, manufacturers and distributors of 1¼-grain size aspirin tablets discontinue the distribution of such tablets in retail containers containing more than 36 tablets, to reduce the hazard of accidental poisoning;

(3) The flavoring of 5-grain aspirin tablets or other "adult aspirin tablets" be discontinued; and

(4) Labeling giving undue emphasis to the pleasant flavor of flavored aspirin tablets be discontinued.

(d) Salicylate preparations other than aspirin tablets sold as such may, at the option of the distributor, be labeled for use by adults only. If their labeling and advertising clearly offer them for administration to adults only.

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